REMARKS/ARGUMENTS

The claims 17 and 30-44 were pending and examined. The claims have been amended as noted above. Reexamination and reconsideration of the claims, as amended, are respectfully requested.

Independent claim 17, as well as all claims dependent thereon, were rejected as being obvious over the combination of Beyerlein '297 as modified by Leclerc '197. Such rejections are traversed in part and overcome in part.

The Examiner relies on Fig. 9 of Beyerlein to teach injecting a pharmaceutical agent beyond the EEL of a coronary blood vessel by 5 mm or less and confirming the needle position. Applicants respectfully disagree with this characterization.

Beyerlein teaches advancing a needle fully from a delivery catheter and confirming that the delivery catheter is closely positioned against the blood vessel wall, as described in, for example, paragraph [0056]. Thus, while Beyerlein may describe confirming the position of the needle with respect to the blood vessel lumen, it does not teach or suggest confirming that the needle has extended beyond the EEL of a coronary blood vessel by any distance.

The Examiner does concede that Beyerlein fails to teach confirming the needle position "by injecting contrast media through the needle aperture" and relies on Leclerc to teach this step. Such reliance is misplaced. Paragraph [0107] of Leclerc, relied on by the Examiner, reads as follows:

> ***[0107]*** *The radioactive oligonucleotide of the present invention, more particularly a 15-mer single strand DNA molecule, was used as a molecular delivery mode of ß-particles to target specifically vascular cells. The ^{32}P-oligonucleotide, highly stable in the presence of cell layers (Fareh J, et al., Circulation, 99 (11):1477-1484, 1999), was designed with phosphorothioate bonds to increase its physical stability. The Infiltrator® catheter (InterVentional Technologies, San Diego, Calif.) was used for a site-specific administration of the ^{32}P-oligonucleotide. The exact location of infiltrator® balloon was verified and recorded with an injection of contrast media. After proper positioning of the drug delivery device at the selected site, the balloon was inflated to 2-4 atmospheres. The adequate apposition of the needles within the vessel wall was verified with*

contrast media. A total bolus of 0.6 mL of ^{32}P-oligonucleotide, diluted in contrast media, was then slowly infused over 60-90 seconds, with continuous monitoring of ECG to assess any sign of ischemia. Following balloon deflation, control angiography was performed to document any residual luminal stenosis or vessel wall dissection. If spasm was documented, 1 mL of nitroglycerin solution at a concentration of 0.3 mg/mL was injected intra-coronary.

Thus, Leclerc teaches that the axial position of the drug delivery device is confirmed, not the penetration distance of any needle on the delivery catheter. Indeed, the Infiltrator® catheter includes a balloon with a plurality of infusion nipples over its surface. The infusion nipples have a very short length, about 0.25 mm, and are not intended to penetrate through the arterial wall into the adventitial tissue. A complete description of the Infiltrator® catheter is provided in Barath (1997), attached hereto. See the device description on page 334 which describes the nipple length of 0.25mm.

The teaching in paragraph [0107] of Leclerc is only that "adequate apposition of the needles within the vessel wall was verified with contrast medium." One skilled in the art would assume that this meant that the physician looked for leakage or flow of the contrast media down the blood vessel. If such leakage or flow was not observed, it can be assumed that the balloon "apposes" the luminal wall and the drug was being delivered into the vessel wall as intended. As the Infiltrator® catheter is not even capable of advancing the delivery nipples into the EEL, Leclerc cannot be assumed to teach or suggest confirmation of such needle penetration.

Nonetheless, in order to expedite prosecution of the present application, Applicants have amended independent claim 17, the only pending independent claim, to further recite that the catheter is first positioned longitudinally within the lumen of the blood vessel and then that a needle is advanced radially outward from the blood vessel through the blood vessel wall and past the EEL. Confirmation that the delivery aperture of the needle has radially penetrated into the adventitial tissue beyond the EEL is then confirmed by observing one of two distinct flow patterns, neither of which is taught or suggested by Leclerc. If the contrast media spreads longitudinally along the outside of the vessel wall, the presence of the aperture of the needle in the adventitial tissue has been confirmed. If, however, the media is constrained within the wall of the blood vessel, it is clear that the needle aperture has not reached the adventitial

tissue. Neither of these flow patterns nor their significance with respect to radial needle penetration is remotely taught or suggested in Leclerc.

For these reasons, Applicants respectfully submit that independent claim 17, as amended, as well as all claims dependent thereon, are now in condition for allowance.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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Attachment: Barath (1997) Cath. Cardio. Diagn. 41:333-341.
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